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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/784,232      | 02/24/2004  | Yoshiharu Hayashi    | 2004_0298           | 8348             |

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EXAMINER

STOCKTON, LAURA LYNNE

|          |              |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
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1626

DATE MAILED: 12/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/784,232

Applicant(s)

HAYASHI ET AL.

Examiner

Laura L. Stockton, Ph.D.

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☒ Certified copies of the priority documents have been received in Application No. 09/091,993.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 2/24/04.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_.

## DETAILED ACTION

Claims 1-24 are pending in the application.

### *Priority*

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/091,993, filed on June 26, 1998.

### *Information Disclosure Statement*

The Information Disclosure Statement filed on February 24, 2004 has been considered by the Examiner.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 6 is rejected under 35 U.S.C. 102(b) as being anticipated by Sumiyoshi et al. {Annals of the New York Academy of Sciences, (January 17, 1995), Vol. 748, pages 74-85}.

Sumiyoshi et al. disclose that compound Y-20811 is known to have a long-lasting and selective inhibitory effects on thromboxane A<sub>2</sub> synthetase and brings about biological effects such as inhibition of platelet aggregation, antithrombotic effect and antivasospastic effects of coronary artery (page 74).

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oda et al. {U.S. Pat. 5,091,191}, Tsuruda et al. {U.S. Pat. 4,661,603}, Kudome et al. {JP 63-119425, see English translation}, Sumiyoshi et al. {Annals of the New York Academy of Sciences, (January 17, 1995), Vol. 748, pages 74-85} and Tsuruda et al. {J. Pharm. Soc. of Japan, Yakugaku Zasshi, January 1989, Vol. 109, No. 1, pages 26-32 – see English translation} each in view of the teachings in Matsui et al. {JP 03-7281, see English translation}, Erdbrugger et al. {Prostaglandins in Clinical Research: Cardiovascular System, pages 389-394, 1989}, Sone et al. {Life Sciences, Vol. 58, No. 3, pages 239-243, 1996} and Patrono et al. {J. of Lipid Mediators, 6 (1993), pages 411-415}.

*Determination of the scope and content of the prior art (MPEP §2141.01)*

Applicants claim methods of prophylaxis and treatment of diabetic ophthalmopathy and diabetic arteriosclerosis by administering an

effective amount of 4-[ $\alpha$ -hydroxy-2-methyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid, an optically active compound thereof or a pharmaceutically acceptable salt thereof or hydrate thereof.

Oda et al. (column 1, lines 6-22), Tsuruda et al. '603 (column 4, lines 67-68; and column 5, lines 1-14 and 63-65), Kudome et al. (pages 2 and 3 of the English translation), Sumiyoshi et al. (page 74) and Tsuruda et al. '1989 (page 1 of the English translation) each disclose that the sodium salt/dihydrate of 4-[ $\alpha$ -hydroxy-2-methyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid and (-)-compounds of sodium salt  $\frac{2}{3}$ -dihydrate thereof inhibit the biosynthesis of the enzyme of thromboxane A<sub>2</sub>.

*Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)*

However, Oda et al., Tsuruda et al. '603, Kudome et al. and Tsuruda et al. '1989 do not teach or suggest that 4-[ $\alpha$ -hydroxy-2-methyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid, an optically active compound thereof or a pharmaceutically acceptable salt thereof or

hydrate thereof, are useful in the treatment of diabetic ophthalmopathy and diabetic arteriosclerosis.

*Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)*

Matsui et al. (pages 2 and 3 of the English translation) and Sumiyoshi et al. (page 74) teach imidazole compounds which inhibit the synthesis of the enzyme of thromboxane  $A_2$  and are useful in the treatment of diabetes, arteriosclerosis, asthma, etc.

Erdbrugger et al. (page 389 and 393) teach that diabetes is known to be an important risk factor of arteriosclerosis and that when vascular endothelial cells are exposed to said risk factor, the quantity of prostaglandin  $E_2$  decreases and the synthesis of thromboxane  $A_2$  is accelerated which plays an important role in the initial phase of arteriosclerosis formation.

Sone et al. (page 239) teach that the synthesis of thromboxane  $A_2$  contributes to the progression of ophthalmopathy.

Patrono et al. (pages 411 and 413-414) teach that the relationship between familial heart and blood diseases and that of growth and

regulation thereof of the thromboxane  $A_2$  can be a therapy of blood vessel and kidney complications related to these diseases.

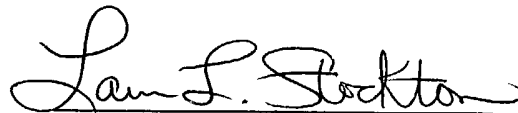
Since it is recognized in the secondary references, and in the case of primary reference Sumiyoshi et al., that ophthalmopathy, arteriosclerosis, nephropathy and neuropathy, as complications of diabetes, and can be treated by inhibiting the synthesis of thromboxane  $A_2$ , one skilled in the art would expect that the compounds disclosed in Oda et al., Tsuruda et al. '603, Kudome et al., Sumiyoshi et al. and Tsuruda et al. '1989, which inhibit the synthesis of thromboxane  $A_2$ , would also be useful in the treatment of complications of diabetes. Therefore, the instant claimed invention would have been obvious and suggested to one skilled in the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:15 am to 2:45 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.



Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Official fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

A handwritten signature in cursive script, reading "Laura L. Stockton".

Laura L. Stockton, Ph.D.  
Patent Examiner  
Art Unit 1626, Group 1620  
Technology Center 1600

December 9, 2004